

Claims:

1. A method of continuous titration in which at least one parameter of at least one compound in a test mixture may be monitored as the composition of the mixture
5 is continuously varied by changing the concentration of one or more species in the mixture, the method comprising the steps of continuously mixing at least two component fluid streams to form a test mixture stream and passing the test mixture stream through a spectrophotometric detection zone, characterised in that the volume to volume ratio of at least two of the component streams forming
10 the test mixture stream is continuously and linearly varied with time by alteration of the relative proportions of the component streams forming the test mixture, whilst the total volume of the test mixture stream remains constant.
2. A method according to claim 1 wherein the test mixture stream is formed from
15 three component fluid streams, the proportion of one component fluid stream remaining constant, the proportions of the second and third component fluid streams being variable in inverse proportion to one another.
3. A method of continuous titration comprising mixing a flowing fluid stream
20 comprising a compound under test with at least one additional flowing fluid stream to form a test mixture stream and passing the test mixture stream through a spectrophotometric detection zone at which readings relating to at least one physical or chemical parameter of the compound under test are taken, characterised in that the test mixture stream is passed through the
25 spectrophotometric detection zone at a constant flow rate and that the flow rate of at least two of the flowing fluid streams forming the test mixture stream is continuously and linearly varied with time.
4. A method according to claim 1 or claim 2 wherein the variable component
30 streams comprise buffer solutions, test reagents, aqueous or organic solvents.
5. A method according to claim 4 wherein there are at least two variable components, comprising two linearising buffer solutions.
- 35 6. An analytical device comprising;

- a) at least two input ports in fluid communication with a common channel;
- b) a detection zone having an input in fluid communication with the common channel and an output;
- c) a spectrophotometric detector for monitoring fluid flowing through the detection zone and producing data relating to at least one chemical or physical characteristic of the fluid; and

5 d) control means associated with the input ports for controlling the relative amounts of fluid introduced into the common channel through each port to vary the composition of the fluid in the common channel continuously and linearly with time.

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- 7. An analytical device according to claim 6 wherein the spectrophotometric detector is an ultraviolet or visible range spectrophotometer, a fluorimeter, a polarimeter, a colourimeter, or a light scattering, optical rotation or circular dichroism detector.
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- 8. An analytical device according to claim 7 wherein the spectrophotometric detector is an ultraviolet or visible range spectrophotometer.
- 20 9. An analytical device according to any one of claims 6 to 7 wherein the control means associated with the input ports comprises an automatic syringe, mixer pump, peristaltic pump or digital on-off valve pump, or a combination thereof.
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- 10. An analytical device according to any one of claims 6 to 9 further comprising an automated sample delivery device adapted to deliver a plurality of samples successively into the common channel.
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- 11. An analytical device according to claim 10 wherein the automated sample delivery device comprises an autosampler.
- 12. An analytical device according to any one of claims 6 to 11 for use in the high-throughput determination of pKas.
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- 13. A method according to claim 5 wherein the linearising buffers are formed from acidic and basic components derived from the same compound such that the

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overall chemical composition of the test mixture stream remains constant during titration as the relative proportions of the two linearising buffers are changed.

14. A method according to claim 13 wherein the acidic and basic components
5 include citric acid, potassium citrate, KH_2PO_4 , K_2HPO_4 , HCl and KOH.